Quidel Corporation

QuickVue® H. pylori gII
Waived Procedure Manual

Procedure:

Prepared by	**Date Adopted**	**Supercedes Procedure #**

Review Date	**Revision Date**	**Signature**

Distributed to	**#of Copies**	**Distributed to**	**#of Copies**

This Procedural Bulletin is intended to provide a ready outline reference for performance of the assay. These abbreviated directions for use are not intended to replace the complete package insert. It is the obligation of every manufacturer of medical devices labeled FOR *IN VITRO* DIAGNOSTIC USE to provide a complete package insert in accordance with FDA labeling regulation (21CFR809.10). Prepared in accordance with the guidelines recommended by the National Committee for Clinical Laboratory Standards, Villanova, PA 19085; NCCLS Document GP2-A2.

QuickVue® H. pylori gII
Waived Procedure Manual

INTENDED USE
The QuickVue H. pylori gII is a lateral-flow immunoassay intended for the rapid, qualitative detection of IgG antibodies specific to *Helicobacter pylori* in human serum or plasma as an aid in the diagnosis of *H. pylori* infection in patients with clinical signs and symptoms of gastrointestinal disease. The test is intended for use by health care professionals.

SUMMARY AND EXPLANATION
Helicobacter pylori is implicated in the etiology of a variety of gastrointestinal diseases, including non-ulcer dyspepsia, duodenal and gastric ulcer, and active and chronic gastritis[1,2]. Recent studies also suggest an association of *H. pylori* infection with stomach cancer; the role of *H. pylori* and the factors involved in the development of these diseases are still under investigation[3].

Several treatment regimens using antibiotics in combination with bismuth compounds have been shown to be effective in treating active *H. pylori* infection[4,5]. Successful eradication of *H. pylori* is associated with clinical improvement in patients with chronic active gastritis, gastric ulcer and duodenal ulcer[4,5].

Individuals infected with H. pylori develop serum antibodies which correlate strongly with histologically confirmed H. pylori infection[6,7,8]. The QuickVue H. pylori gII detects *H. pylori*-specific IgG antibodies produced by individuals colonized or infected with the organism. The QuickVue H. pylori gII is simple to perform, requires no instrumentation and yields rapid, qualitative test results in minutes.

PRINCIPLE OF THE TEST
To perform the test, approximately 50 µL of whole blood is added to the Test Cassette. If the patient sample contains *H. pylori*-specific IgG antibodies, a faint pink-to-red Test Line will be visible in the Result Window along with a blue procedural Control Line, indicating a positive result. If *H. pylori*-specific IgG antibody is not present or is present at very low levels in the patient sample, only a blue procedural Control Line will be visible. If the blue procedural Control Line does not develop within 5 minutes, the test is considered invalid.

QuickVue® H. pylori gII
Waived Procedure Manual

REAGENTS AND MATERIALS SUPPLIED:

- Test Cassettes (10 or 30): Murine monoclonal antibody to human IgG (Test Line) and rabbit polyclonal antibody (Control Line).
- Disposable Droppers (10 or 30)
- Capillary Tubes (10 or 30)
- Positive Control (1): Diluted human plasma containing *H. pylori*-specific IgG, 0.1% thimerosal.
- Negative Control (1): Diluted human plasma, 0.1% thimerosal.
- Direction Insert (1)
- Procedure Card (1)

WARNINGS AND PRECAUTIONS:

- For *In Vitro* Diagnostic Use.
- Do not use kit contents after the expiration date printed on the outside of the box.
- Use appropriate precautions in the collection, handling, storage and disposal of the specimens and used kit contents. Discard used materials in a proper biohazard container.
- The Test Cassette must remain sealed in the protective foil pouch until just prior to use.
- To obtain accurate results, you must follow the Direction Insert instructions.

KIT STORAGE AND STABILITY:

Store kit at room temperature 59-86°F (15-30°C) out of direct sunlight. Do not freeze. Kit contents are stable until the expiration date printed on the outer box.

SPECIMEN COLLECTION AND STORAGE:

Whole Blood:
Collect an anticoagulated blood sample [sodium heparin (green-top tubes), lithium heparin (green-top tubes) or potassium EDTA (lavender-top tubes)] following standard laboratory procedures. Whole blood samples may be stored up to 4 hours at room temperature or either on ice or refrigerated (2-8°C) for up to 72 hours prior to testing.

Fresh Capillary Blood Sample:
To use a capillary tube

- Ensure that the finger is clean, dry and warm.
- Puncture the side of the middle or ring finger skin with the lancet. Wipe away the first sign of blood.
- Gently rub the hand from palm to finger to obtain a rounded drop of blood.
- Touch the capillary tube to the blood until filled to the black line (Do not squeeze the bulb at the end of the capillary tube while obtaining the sample).
- Squeeze the bulb end of the capillary tube to dispense the whole blood sample.

To use hanging drop

- Ensure that the finger is clean, dry and warm.
- Puncture the side of the middle or ring finger skin with the lancet. Wipe away the first sign of blood.
- Gently rub the hand from palm to finger to obtain a rounded drop of blood.
- Position the finger so that the drop of blood is just above the Sample Well of the Test Cassette.

TEST PROCEDURE:

All test materials and patient samples must be at room temperature before beginning.

Note: *Sample volumes of less than 1 drop may yield an incorrect result.*

Test Procedure: Remove the Test Cassette from the foil pouch. Place it on a clean, dry, level surface.

Add 1 drop of anticoagulated WHOLE BLOOD using a clean disposable dropper to the round Sample Well on the Test Cassette.

The Test Cassette should not be moved until the assay is complete and ready for interpretation.

Add 1 CAPILLARY TUBE of WHOLE BLOOD from a fingerstick to the round Sample Well on the Test Cassette.

The Test Cassette should not be moved until the assay is complete and ready for interpretation.

Add 2 hanging drops of WHOLE BLOOD from a fingerstick to the round Sample Well on the Test Cassette. Allow 2 drops of blood to fall into the center of the Sample Well, or move the patient's finger so that the drop

touches the center of the Sample Well. Avoid touching the finger directly to the center of the Sample Well.

The Test Cassette should not be moved until the assay is complete and ready for interpretation.

READ RESULTS AT 5 MINUTES. Some positive results may be seen earlier.

INTERPRETATION OF RESULTS:

Refer to Procedure Card for interpretation of test results.

Positive Result

Any shade of a pink-to-red Test Line near the letter "T" and a blue procedural Control Line near the letter "C" within 5 minutes indicates the presence of *H. pylori* -specific IgG antibodies.

Negative Result

Only a blue procedural Control Line near the letter "C" at 5 minutes indicates the absence of *H. pylori*-specific IgG antibodies.

Invalid Result

The test result is considered invalid if the blue procedural Control Line is not visible at 5 minutes after sample application, even if the Test Line is visible. If the result is invalid, retest using a new Test Cassette or contact the toll-free Technical Assistance Line.

QuickVue® H. pylori gII
Waived Procedure Manual

QUALITY CONTROL:

Built-in Quality Control Features

The QuickVue H. pylori gII contains built-in control features. The manufacturer's recommendation for daily quality control is to document the performance of the built-in controls for the first sample tested each day.

The two-color result format provides a clear-cut readout for positive and negative results. The appearance of a blue procedural Control Line provides several forms of internal control: (1) capillary flow occurred; and (2) functional integrity of the test strip was maintained. If the blue procedural Control Line does not develop at 5 minutes, the test result is considered invalid.

A built-in negative control is provided by the clearing of red background color, verifying that the test has been performed correctly. The result area should be white-to-light pink within 5 minutes and not interfere with interpretation of the test result. If background color appears which interferes with interpretation of the test result, the result is considered invalid. Should this occur, review the procedure and repeat the test with a new Test Cassette.

External Controls

External controls may also be used to demonstrate that the reagents and assay procedure performed properly. Positive and Negative Control Solutions are supplied with the kit. Add **two drops** of the Positive or Negative Control Solution to the Sample Well using a new Test Cassette; continue with the assay as described in the **Test Procedure** using these controls in place of a patient sample.

A positive and negative external control must be tested when opening a new test kit. Each operator performing testing within a test kit must test a positive and negative external control once with each test kit.

If the Positive and Negative Controls do not perform as expected, repeat the test or contact QUIDEL Technical Assistance before testing patient samples.

QuickVue® H. pylori gII
Waived Procedure Manual

LIMITATIONS:

The contents of this kit are for use in the qualitative detection of *H. pylori*-specific IgG antibodies and do not indicate the titer of the antibody in the sample. The test should be used only to evaluate adult patients with clinical signs and symptoms suggestive of gastrointestinal disease.

The test is not intended for use with asymptomatic patients. Performance characteristics for persons under the age of 18 have not been established with this test.

A positive QuickVue result only indicates the presence of specific IgG antibodies to *H. pylori*, but determination of an active or inactive infection cannot be made.

A negative QuickVue result indicates that *H. pylori*-specific IgG antibody is not present, or is present at a level below the detection threshold of the test.

Test results must always be evaluated with other data available to the physician. Additional follow-up testing is recommended if the QuickVue result is negative and *H. pylori* infection is suspected.

EXPECTED VALUES:

In the United States, approximately 11% of symptomatic individuals with normal gastric histology have been reported to be colonized with *H. pylori*, while 63% of those with chronic gastritis yielded positive culture biopsies. The factors that lead from colonization with the organism to infection are unknown.

The prevalence rate of colonization appears to be age related with 50% of adults shown to be colonized with the organism by age sixty. Eighty to 100% of individuals with signs and symptoms of other gastrointestinal conditions such as duodenal ulcers, are reported to be positive for *H. pylori* infection[9].

QuickVue® H. pylori gII
Waived Procedure Manual

PERFORMANCE CHARACTERISTICS:

Clinical Sensitivity, Specificity, and Accuracy

The performance of the QuickVue H. pylori gII was determined in a multi-center clinical evaluation. Serum specimens were obtained from 342 patients undergoing endoscopic examination.

For this study, each patient was evaluated by the QuickVue H. pylori gII, an EIA *H. pylori* antibody detection assay and histology and/or culture.

Table 1 presents a comparison of the QuickVue H. pylori gII to biopsy (culture and/or histology).

TABLE 1

		Biopsy	
		Pos	Neg
QuickVue H. pylori gII Test Result	Pos	158	36
	Neg	18	130

Sensitivity:	158/176	90% [95% C.I. 86%-93%]
Specificity:	130/166	78% [95% C.I. 73%-82%]
PPV:	158/194	81%
NPV:	130/148	88%
Agreement:	288/342	84%

The 36 QuickVue positive, biopsy negative specimens were tested by an EIA *H. pylori* antibody detection assay. Three (3) specimens were equivocal and 21 were positive, indicating the presence of *H. pylori*-specific IgG antibodies in those specimens.

The 18 QuickVue negative, biopsy positive specimens were tested by an EIA *H. pylori* antibody detection assay. Two (2) were equivocal and 9 were negative by EIA, indicating the absence of *H. pylori*-specific IgG antibodies in those specimens.

The QuickVue H. pylori gII was also compared directly to an EIA *H. pylori* antibody detection assay. Because sampling errors may occur during biopsy due to the sporadic distribution of the bacteria in the gastric mucosa, the actual bacteria may not be sampled during biopsy, making it difficult to detect the bacterium by histology. Antibody detection tests, therefore, are more likely to determine if an infection is present, provided that the patient is not immuno-suppressed and is actually producing antibodies to *H. pylori*. In this study, the overall agreement between the two tests was 92%. Table 2 presents the results of this study.

TABLE 2

		EIA	
		Pos	Neg
QuickVue H. pylori gII Test Result	Pos	174	14
	Neg	12	128

Cross-Reactivity
Sera containing known amounts of antibodies to *H. pylori* were tested with *C. jejuni, C. fetus, C. coli* and *E. coli*. All species tested showed no cross-reactivity, indicating that the QuickVue H. pylori gII has a high degree of specificity for human antibodies to *H. pylori*.

Interference Studies
QuickVue H. pylori gII results were not affected by elevated levels of serum albumin, bilirubin or hemoglobin. Altering the hematocrit ranging from 20 to 60% did not affect the accuracy of the test.

Reproducibility Studies
The within-run and between-run performance of the QuickVue H. pylori gII was evaluated using negative, low positive and high positive samples for antibodies to *H. pylori*. All results obtained were 100% in agreement with the expected results.

Physician's Office Laboratory (POL) Studies
An evaluation of the QuickVue H. pylori gII was conducted at three Physicians' Offices using a panel of coded specimens. Testing was performed by physician office personnel with diverse educational backgrounds and work

experience at three different locations. The proficiency panel contained negative, moderate positive and high positive specimens. Each specimen level was tested a minimum of six replicates at each site over a period of three days.

The results obtained at each site agreed 100% with the expected results. No significant differences were observed within run (6 replicates), between runs (3 different assay days) or between sites (3 different POL sites).

COMMENTS AND TECHNICAL ASSISTANCE:
If you have any questions regarding the use of this product, please call QUIDEL's Technical Assistance Number 800-874-1517 (toll-free) or 858-552-1100, Monday through Friday, between 7:00 a.m. and 5:00 p.m., Pacific Time. If outside the United States contact your local QUIDEL office or distributor.

REFERENCES:

1. Marshall, BJ, McGechie, DB, Rogers, PAR and Glancy, RG. Pyloric Campylobacter infection and gastroduodenal disease. Med. J. Australia. 149: 439-44; 1985.

2. Soll, AH. Pathogenesis of peptic ulcer and implications for therapy. New Engl. J. Med. 322: 909-916; 1990.

3. Parsonnet, J, Freidman, GD, Vundersteen, DP, Chang, Y, Vogelman, JH, Orentreich, N and Sibley, RK. Helicobacter pylori infection and the risk of gastric carcinoma. New Engl. J. Med. 325: 1127-31; 1991.

4. Marshall, BJ, Warren, JR and Blincow, ED. Prospective double-blind trial of duodenal ulcer relapse after eradication of Campylobacter pylori. Lancet. December 1437-42; 1988.

5. Graham, DY et al. Effect of treatment of Helicobacter pylori infection on the long-term recurrence of gastric or duodenal ulcer. Annals of Internal Med. 116: 705; 1992.

6. Ansorg, R, Von Recklinghausen, G, Pomarius, R and Schmid, EN. Evaluation of techniques for isolation, subcultivation and preservation of Helicobacter pylori. J. Clin. Micro. 29: 51-53; 1991.

7. Pronovost, AP, Rose, SL, Pawlak, J, Robin, H and Schneider, R. Evaluation of a new immunodiagnostic assay for Helicobacter pylori antibody detection. Correlation with histopathological and microbiological results. J. Clin. Microbiol. 32: 46-50; 1994.

8. Megraud, F, Brassens-Rabbe, MP, Denis, F, Belbouri, A and Hoa, DQ. Seroepidemiology of Campylobacter pylori infection in various populations. J. Clin. Microbiol. 27: 1870-3; 1989.

9. Perez-Perez, G, Dworkin, B, Chodos, J, Blaser, M. Campylobacter pylori antibodies in humans. Annals of Internal Med. 109: 11-17; 1988.

QuickVue® H. pylori gII
Waived Procedure Manual

Log Sheet QuickVue ® H. pylori gII

Lot Number: _____
Exp. Date: _____

Record Built-In Positive and Negative Controls. Refer to Quality Control Section.

	Date	Patient Name	Positive Procedural Control (Blue Line in Control Window)	Negative Procedural Control (Background = no interference)	Test Result at 5 min.	Tech.
1						
2						
3						
4						
5						
6						
7						
8						
9						
10						